

WEST Search History

DATE: Wednesday, January 17, 2003

<u>Set Name</u> side by side	<u>Query</u>	<u>Hit Count</u>	<u>Set Name</u> result set
<i>DB=USPT,PGPB,JPAB,EPAB,DWPI; PLUR=NO; OP=OR</i>			
L19	L18 and immunis\$4	3	L19
L18	L17 and library	170	L18
L17	heavy adj chain adj immunoglobulin	289	L17
L16	L14 and vhh	1	L16
L15	L14 and immunis\$5	1	L15
L14	L13 and (light adj chain)	186	L14
L13	L12 and camel\$5	187	L13
L12	(expression near2 library) and l1	387	L12
L11	L10 and camel\$5	211	L11
L10	L8 and (light adj chain)	211	L10
L9	L8 and immunised	3	L9
L8	L7 and camel\$5	212	L8
L7	l1 and library	1027	L7
L6	l1 and camel?	11	L6
L5	L4 and library	43	L5
L4	cameli\$5 and (immunoglobulin or antibody)	80	L4
L3	cameli\$5 and (immunoglobulin or antibody)	80	L3
L2	L1 and camelid	13	L2
L1	heavy adj3 immunoglobulin	1419	L1

END OF SEARCH HISTORY

(FILE 'HOME' ENTERED AT 11:48:41 ON 22 JAN 2003)

FILE 'MEDLINE, CAPLUS' ENTERED AT 11:48:57 ON 22 JAN 2003

L1 193 S HEAVY CHAIN IMMUNOGLOBULIN#
L2 5 S CAMEL? AND L1

FILE 'STNGUIDE' ENTERED AT 11:50:40 ON 22 JAN 2003

FILE 'MEDLINE, CAPLUS' ENTERED AT 11:51:23 ON 22 JAN 2003

L3 28 S (EXPRESSION LIBRARY) AND REPERTOIRE
L4 752 S LIBRARY AND REPERTOIRE
L5 170 S L4 AND (HEAVY CHAIN)
L6 147 S L5 AND IMMUNOGLOBULIN#
L7 6 S L6 AND CAMEL?

FILE 'STNGUIDE' ENTERED AT 11:57:16 ON 22 JAN 2003

FILE 'MEDLINE, CAPLUS' ENTERED AT 12:01:11 ON 22 JAN 2003

L8 2 S (EXPRESSION LIBRARY) AND REPERTOIRE AND (HEAVY CHAIN)
E FRENKEN LEON/AU
L9 32 S E1-E7
L10 2 S L9 AND REPERTOIRE

L2 ANSWER 4 OF 5 MEDLINE
 AN 95132591 MEDLINE
 DN 95132591 PubMed ID: 7831284
 TI Sequence and structure of VH domain from naturally occurring **camel heavy chain immunoglobulins** lacking light chains.
 AU Muyldermans S; Atarhouch T; Saldanha J; Barbosa J A; Hamers R
 CS Vrije Universiteit Brussel, Instituut voor Moleculaire Biologie, Sint Genesius Rode, Belgium.
 SO PROTEIN ENGINEERING, (1994 Sep) 7 (9) 1129-35.
 Journal code: 8801484. ISSN: 0269-2139.
 CY ENGLAND: United Kingdom
 DT Journal; Article; (JOURNAL ARTICLE)
 LA English
 FS Priority Journals
 EM 199502
 ED Entered STN: 19950307
 Last Updated on STN: 19950307
 Entered Medline: 19950217
 AB We cloned 17 different PCR fragments encoding VH genes of **camel** (*Camelus dromedarius*). These clones were derived from the **camel heavy chain immunoglobulins** lacking the light chain counterpart of normal immunoglobulins. Insight into the **camel** VH sequences and structure may help the development of single domain antibodies. The most remarkable difference in the **camel** VH, consistent with the absence of the VL interaction, is the substitution of the conserved Leu45 by an Arg or Cys. Another noteworthy substitution is the Leu11 to Ser. This amino acid normally interacts with the CH1 domain, a domain missing in the **camel heavy chain immunoglobulins**. The nature of these substitutions agrees with the increased solubility behavior of an isolated **camel** VH domain. The VH domains of the **camels** are also characterized by a long CDR3, possibly compensating for the absence of the VL contacts with the antigen. The CDR3 lacks the salt bridge between Arg94 and Asp101. However, the frequent occurrence of additional Cys residues in both the CDR1 and CDR3 might lead to the formation of a second internal disulfide bridge, thereby stabilizing the CDR structure as in the DAW antibody. Within CDRs of the **camel** VH domains we observe a broad size distribution and a different amino acid pattern compared with the mouse or human VH. Therefore the **camel** hypervariable regions might adopt structures which differ substantially from the known canonical structures, thereby increasing the repertoire of the **camel** antigen binding sites within a VH.
 CT Check Tags: Animal; Comparative Study; Human; Support, Non-U.S. Gov't
 Amino Acid Sequence
 Binding Sites: GE, genetics
 *Camels: GE, genetics
 *Camels: IM, immunology
 Cloning, Molecular
 Genes, Immunoglobulin
 Immunoglobulin Variable Region: CH, chemistry
 *Immunoglobulin Variable Region: GE, genetics
 Immunoglobulins, Heavy-Chain: CH, chemistry
 *Immunoglobulins, Heavy-Chain: GE, genetics
 Mice
 Molecular Sequence Data
 Molecular Structure
 Polymerase Chain Reaction
 Protein Conformation
 Protein Engineering
 Sequence Homology, Amino Acid
 Species Specificity
 CN 0 (Immunoglobulin Variable Region); 0 (Immunoglobulins, Heavy-Chain)

L7 ANSWER 3 OF 6 MEDLINE
 AN 97462800 MEDLINE
 DN 97462800 PubMed ID: 9323027
 TI Selection and identification of single domain antibody fragments from **camel heavy-chain** antibodies.
 AU Arbabi Ghahroudi M; Desmyter A; Wyns L; Hamers R; Muyldermans S
 CS Vlaams Interuniversitair Instituut voor Biotechnologie, Vrije Universiteit Brussel, Sint Genesius Rode, Belgium.
 SO FEBS LETTERS, (1997 Sep 15) 414 (3) 521-6.
 Journal code: 0155157. ISSN: 0014-5793.
 CY Netherlands
 DT Journal; Article; (JOURNAL ARTICLE)
 LA English
 FS Priority Journals
 EM 199710
 ED Entered STN: 19971224
 Last Updated on STN: 19971224
 Entered Medline: 19971027
 AB Functional **heavy-chain** gamma-immunoglobulins lacking light chains occur naturally in **Camelidae**. We now show the feasibility of immunising a dromedary, cloning the **repertoire** of the variable domains of its **heavy-chain** antibodies and panning, leading to the successful identification of minimum sized antigen binders. The recombinant binders are expressed well in E. coli, extremely stable, highly soluble, and react specifically and with high affinity to the antigens. This approach can be viewed as a general route to obtain small binders with favourable characteristics and valuable perspectives as modular building blocks to manufacture multispecific or multifunctional chimaeric proteins.
 CT Check Tags: Animal; Support, Non-U.S. Gov't
 Amino Acid Sequence
 *Antibodies: GE, genetics
 Antibody Affinity
 Antibody Specificity
 Bacteriophages: GE, genetics
 Binding Sites, Antibody
 *Camels: IM, immunology
 Cloning, Molecular
 Epitope Mapping
 Gene Library
 *Immunoglobulins, Heavy-Chain: GE, genetics
 *Immunoglobulins, Heavy-Chain: IM, immunology
 Immunoglobulins, Heavy-Chain: ME, metabolism
 Molecular Sequence Data
 Polymerase Chain Reaction
 Recombinant Proteins: GE, genetics
 Recombinant Proteins: IM, immunology
 Recombinant Proteins: ME, metabolism
 CN 0 (Antibodies); 0 (Binding Sites, Antibody); 0 (Immunoglobulins, Heavy-Chain); 0 (Recombinant Proteins)

 L7 ANSWER 6 OF 6 CAPLUS COPYRIGHT 2003 ACS
 AN 1998:94336 CAPLUS
 DN 128:242743
 TI The specific variable domain of **camel heavy-chain** antibodies is encoded in the germline
 AU Nguyen, Viet Khong; Muyldermans, Serge; Hamers, Raymond
 CS Department Ultrastructure, Interuniversitair Instituut voor Biotechnologie, Vrije Universiteit Brussel, Sint Genesius Rode, B-1640, Belg.
 SO Journal of Molecular Biology (1998), 275(3), 413-418
 CODEN: JMOBAK; ISSN: 0022-2836
 PB Academic Press Ltd.

DT Journal
 LA English
 CC 15-3 (Immunochemistry)
 Section cross-reference(s): 3

AB The variable domains of the functional **heavy-chain** antibodies (VHs) discovered in **camels** are related to the human VH subgroup III. They are nevertheless clearly distinguishable from the VHs of conventional four-chain Igs by the presence of important amino acid substitutions, located in the solvent-exposed surface normally covered by the variable domain of the light chain. The anal. of an unrearranged dromedary DNA **library** revealed that the specific VHH gene with its characteristic amino acid substitutions is encoded in the germline. Therefore, it is concluded that the VHHs do not arise through an ontogenic process of somatic hypermutation. The presence of putative DNA recombination signals that are more prevalent in the **camel** VHH, compared to the VH germline gene, might play a role in the formation and efficient expansion of the VHH **repertoire**.

ST variable gene **heavy chain** antibody **camel**; Ig **heavy chain** variable sequence **camel**

IT Genetic element
 RL: BOC (Biological occurrence); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); OCCU (Occurrence)
 (RSS (recombination signal sequence); of variable region genes for **heavy-chain** antibodies of **camel**)

IT Leader peptides
 RL: PRP (Properties)
 (for Ig **heavy chain** of **camel**)

IT Antibodies
 RL: BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PROC (Process)
 (**heavy chain**; variable domain of **camel heavy-chain** antibodies is encoded in germline)

IT **Immunoglobulins**
 RL: BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PROC (Process)
 (heavy chains; variable domain of **camel heavy-chain** antibodies is encoded in germline)

IT Protein sequences
 (of **heavy-chain** antibody variable domain of **camel**)

IT DNA sequences
 (of variable region genes for **heavy-chain** antibodies of **camel**)

IT Promoter (genetic element)
 RL: PRP (Properties)
 (of variable region genes for **heavy-chain** antibodies of **camel**)

IT Antibody diversity
Camel (**Camelus** dromedarius)
 V(D)J recombination
 (variable domain of **camel heavy-chain** antibodies is encoded in germline)

IT Gene, animal
 RL: BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PROC (Process)
 (variable domain of **camel heavy-chain** antibodies is encoded in germline)

IT 204870-18-8, GenBank AF000603 204870-19-9, GenBank AF000604
 RL: PRP (Properties)
 (nucleotide sequence; variable domain of **camel heavy-chain** antibodies is encoded in germline)

L8 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2003 ACS

AN 2000:513796 CAPLUS

DN 133:130765

TI Construction of a camelid Ig **heavy chain** variable region **expression library** for production of antibody fragments

IN Frenken, Leon Gerardus Joseph; Van der Logt, Cornelis Paul Eric

PA Unilever Plc, UK; Unilever Nv; Hindustan Lever Limited

SO PCT Int. Appl., 60 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000043507	A1	20000727	WO 2000-EP296	20000113
	W:	AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
	RW:	GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
	EP 1144616	A1	20011017	EP 2000-901571	20000113
	R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO			
	US 6399763	B1	20020604	US 2000-487253	20000119
PRAI	EP 1999-300351	A	19990119		
	WO 2000-EP296	W	20000113		

RE.CNT 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2003 ACS

AN 1999:487325 CAPLUS

DN 131:115301

TI Expression libraries of **heavy chain** antibodies

IN Frenken, Leo Gerardus Joseph; Van der Logt, Cornelis Paul Erik

PA Unilever PLC, UK; Unilever N. V.; Hindustan Lever Limited

SO PCT Int. Appl., 32 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9937681	A2	19990729	WO 1999-EP481	19990125
	WO 9937681	A3	19991014		
	W:	AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
	RW:	GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
	AU 9935965	A1	19990809	AU 1999-35965	19990125
	BR 9907241	A	20001017	BR 1999-7241	19990125
	EP 1051493	A2	20001115	EP 1999-917814	19990125
	R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, NL, SE, PT, IE, FI			
PRAI	EP 1998-300525	A	19980126		

WO 1999-EP481

W

19990125